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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/660,568	09/11/2000	David Ralph	UROC:014USD1	1840

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/660,568	RALPH ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-13,15-26,64 and 65* is/are pending in the application.

4a) Of the above claim(s) *21-26 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13,15,16,18-20 and 64* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/26/06 has been entered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-13, 15, 16, 18-20 and 64 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The instant invention is broadly drawn to the detection of metastatic cancer via the detecting of disease markers expressed in peripheral blood and diagnosing the disease state via the detection. The scope includes the detection of markers for metastatic cancers including breast and prostate cancers. The specification, as filed, discloses 7 "markers" (nucleic acid sequences) associated with metastatic prostate cancer that are expressed in peripheral blood of prostate cancer patients. The specification identifies specific IL-8 and IL-10 sequences among the 7 "markers" whose expression in peripheral blood is associated with metastatic prostate cancer. The specification provides no other examples of any other "markers" that may be associated with any particular gene for use in the instantly claimed invention.

With the exception of the markers indicated above the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides markers required to perform the instant methods regardless of the complexity or simplicity of the method of isolation. The instant specification does not provide "markers" other than those indicated above and one in the art, based on the structure of those would not be able to envision the structure (sequence) of any other "markers" (mRNA) that may be associated with any particular disease within the broad scope of diseases considered in the instant invention. Without a description of such markers, one in the art would not be

able to produce primers or probes for any particular marker associated with any particular disease, for example. The specification further does not provide any other disease states that may be determined via the increase or decrease in expression of the 7 "markers" identified in the specification, for example.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using

"such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the

patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

The instant specification provides guidance for one in the art to find markers, but does not describe a representative number to show possession of the claimed invention. The markers disclosed in the specification are associated with prostate cancer, which disclosure does not provide a description of markers for breast cancer or any of the vast number of disease states that would be included in a group described as "a metastatic cancer". The instant specification has not provided any written description of any markers for any disease other than metastatic cancer (prostate). The specification fails to describe those marker sequences that the invention requires to be quantified, for example. The specification fails to provide a correlation between the structure and function of IL-10 or SEQ ID NO: 49 and any other diseases that may be detected by quantification of their expression in peripheral blood, for example.

The instant invention is based on the detection of markers that are differentially expressed in the peripheral blood in a patient with a disease relative to expression in a normal subject. Although the instant specification provides methods of identifying such markers, a sufficient number of markers have not been described to show possession of the broad scope instantly claimed.

Claims 9-13, 15, 16, 18-20 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are rejected for those reasons set forth above. One in the art would clearly require the engagement of vast quantities of trial and error experimentation to determine the markers that may be correlated to the vast range of diseases to be diagnosed in the instant methods.

Applicant's arguments filed 5/26/06 have been fully considered but they are not persuasive. Below is the examiners response to applicants arguments filed 5/26/06 and also arguments set forth in the Examiners answer (applicant points the these arguments in their response).

Applicant argues that the claims s amended have adequate written support and are enabled. Applicant asserts that the invention is based on a diagnostic method involving markers and the examiner is too concerned with what the markers are. Applicant cites case law but does not show how the facts of the case law cited correlates to the instant invention with the exception of *Capon v Eshhar*, 418F.3d 1349, 76 USPQ 2d 1078 (Fed. Cir. 2005). Applicant asserts that in Capon v Eshhar the Federal Circuit ruled that the patentee's directed to chimeric genes was not invalid for failing to describe the diffent chimeras because the invention lays in the novel combination of the DNA segments to achieve a novel result, and not discovering the specific DNA segments. Applicant then argues that their invention is partly based on discovering new markers and also on a new methodology, which is independent of the

specific markers. First, it is unclear to the examiner how the claimed method could be separated from the markers as the markers are required in the claimed method. Secondly, and more importantly, the facts of the instant application and those of Capon v Eshhar are different. If one looks at the invention as described in the Capon v Eshhar it is evident that the invention is made ". . .by combining known antigen-binding-domain producing DNA and known lymphocyte-receptor-protein producing DNA into a unitary gene that can express a unitary polypeptide chain." The instant invention is not composed of known elements. One must first discover the markers in order to perform the full scope of the claimed invention. The markers described in the instant specification do not provide a description of any other markers that may be used in a method to detect metastatic cancer via peripheral blood.

Below are arguments set forth by the examiner in the Examiners answer mailed 3/18/05.

Applicant argues that the claimed invention is directed to a **method of detecting** [emphasis provided by applicant] the quantity of a disease marker mRNA in the peripheral blood and comparing the quantity of the disease marker in a sample with the quantity in a sample with the quantity of the disease marker in normal individual's [peripheral] blood. Applicant asserts the appealed claims do not claim a disease marker, but a method that uses them. The argument appears to be that since the compounds not described are not being claimed no rejection of lack of written description can be made. It would appear that such an argument would represent a semantic distinction

without a difference since the compounds not described are clearly needed in order to practice the claimed method.

Applicant argues that method have been provided to identify markers. Again it is pointed out *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Applicant points to page 8, lines 10-27, for support of a description of the invention. It is noted that the specification provides no disclosure of mRNA markers at the cited location. Applicant points to pages 85-92, which pages provide general teachings for RNA detection processes. The cited pages, 85-92, provide no disclosure of any particular markers in the peripheral blood that are correlated to any particular disease. Applicant also points to the examples at pages 100-161, which disclosure comprises those specific markers clearly acknowledged in the rejections in the Official Actions of record.

It is noted that at page 16, lines 26-30, of the specification it is stated; "Disease states that may be detected by the present method include any disease state for which a marker is known and may include metastatic cancer, particularly metastatic prostate cancer, asthma, lupus. . ." It is the position of the examiner that the only known markers for detection of a disease state via mRNA detection in peripheral blood are those specifically disclosed by applicant and acknowledged in the Official Actions of record. If applicant believes that the prior art provides a sufficient description of other markers for

disease states known to be expressed in the peripheral blood such a disclosure would be taken into consideration.

Applicant argues that "[t]he steps of the **diagnostic method** [emphasis in original] are clear. While the claims may encompass the use of compositions not specifically exemplified or identified, the claims require that there is a difference in the expression of the disease marker mRNA relative to. . ." Applicant argues as if the markers are not essential to practicing the method. The compounds[marker mRNAs] are not ancillary to the method claimed but are integral to its practice. Since the markers of the instant invention are clearly needed to practice the invention and the scope of such markers have not been adequately described, the invention itself [i.e. a method of using the markers] has not been described.

Applicant is also directed to University of Rochester v. G.D. Searle & Co., 69USPQ2d (CA FC 2004). One would not know how to make the claimed substance other than by a trial and error process."" Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods. . .'[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment.'"

Applicant argues that the office action fails to provide a reasonable basis to question the enablement of the instantly claimed methods. Applicant asserts again that the claims are drawn to a method of detection and not to the markers required to perform the methods. Applicant argues as if the markers are not essential to practicing the method. The compounds[marker mRNAs] are not ancillary to the method claimed but are integral to its practice. Applicant argues also that the invention is enabled and argues that written description and enablement are distinct and cite *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). It is the position of the examiner, that although distinct, there is overlap within the written description, enablement and best mode requirements of 112, first paragraph. In the instant case there is clearly overlap since one in the art would require the use of markers that have not been described. One cannot use these markers in the claimed invention when such markers have not been described. Applicant merely provided a trial and error method of finding "markers" where no guidance for what might be the structure and to what diseases they might be related and how a "difference" (increase, decrease, how much of increase or decrease, miss expression, different tissues, temporal . . etc) in expression of such undisclosed structures is to be correlated with any particular disease. The combinations contemplated are astronomical and the guidance provided is limited to seven markers all related to one type of disease. One in the art has been left to *de novo* determine all of the correlations, without any specific guidance for any particular diseases. One in the art has not been provided any particular starting point for what they might look for as a marker, but is left to find such

by trial and error experimentation where there has been no guidance provided such that one would know how or where to look for markers for any particular disease they might wish to detect or diagnose, for example.

The type of experimentation required to practice the invention more broadly than is exemplified is a factor in the enablement analysis, but is not necessarily dispositive. In this case, the more-or-less standard nature of each type of experiment required to expand the scope of the invention is outweighed by the sheer quantity of experimentation required to practice the full scope of the claims, the unpredictability of the art generally (biotechnology) and the claimed method in particular, and the lack of guidance in the specification regarding the direction in which the experimentation should proceed.

Claim 17 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deletes reference to species not elected (SEQ ID NO: 49 is the elected Sequence).

Claims 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 13 recited diseases that expand beyond the scope recited in the base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635